DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

DEC 21 1998

**TRANSMITTED VIA FACSIMILE**

Mr. Stephen Cristo
Assistant Director, Drug Regulatory Affairs
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

**RE: NDA# 19-835**
Zyrtec (cetirizine HCl) Tablets and Syrup
MACMIS ID# 7035

Dear Mr. Cristo:

This letter concerns selected promotional materials for Zyrtec (cetirizine HCl) Tablets and Syrup disseminated by Pfizer, Inc. (Pfizer) (i.e., a bibliography of "Abstracts of Selected Zyrtec Literature"/CL107V98-April 1998 and a detailer "Cytochrome P450 34A or 2D6 Inhibition May Cause Undesirable Levels of Many Drugs—Select drugs metabolized by CYP34A"/TL083R98-April 1998). The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed these materials and concluded that they are misleading and therefore violative of the Federal Food, Drug, and Cosmetic Act and implementing regulations.

Bibliography of "Abstracts of Selected Zyrtec Literature"

The bibliography is a selective collection of literature abstracts summarizing selected Zyrtec clinical study results and conclusions. Pfizer's abstract bibliography is promotional labeling for Zyrtec. The abstract bibliography does not include complete journal articles or study reports; rather it merely states "For full reports, please see your Pfizer or UCB Pharma sales representative."

Most of the abstracts refer to comparative trials in which Zyrtec was concluded to be superior to other antihistamines, while several abstracts refer to off-label dosing for Zyrtec (i.e., 20 mg per day); one suggests an off-label use for Zyrtec in asthma therapy. This collection of clinical study abstracts does not provide sufficient information upon which to base conclusions of safety or efficacy because important methodological and other data underlying the studies are not disclosed in abstract form. The limited information in this abstract bibliography is not adequate substantiation to support promotional claims. Therefore, based on this abstract format, Zyrtec product claims, including safety or efficacy superiority claims in this bibliography, are

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unsubstantiated. Moreover, the Zyrtec abstract bibliography is misleading because it selectively reports on positive/superior Zyrtec outcomes, rather than also reporting on negative or equivocal Zyrtec outcomes. Finally, because of specific methodological issues and limitations pertaining to some of these studies, on previous occasions, DDMAC has objected to Pfizer's use of some of these cited articles as substantiation for various broad efficacy claims or comparative claims in other Zyrtec promotional materials.

Detailer: "Cytochrome P450 34A or 2D6 Inhibition May Cause Undesirable Effects on Plasma Levels of Many Drugs—Select Drugs Metabolized by CYP34A, CYP2D6"

This detailer misleadingly implies that Claritin (loratadine), among various other drugs, causes a risk of serious cardiovascular events when coadministered with other medications because it is metabolized through the Cytochrome P450 pathway. Among the large number of commonly used drugs metabolized through the P450 system, Claritin is misleadingly grouped with a "selected" listing of drugs that are known to present special cardiovascular risks if the patient's Cytochrome P450 system is inhibited (e.g., Hismanal).

Although Claritin is metabolized through the Cytochrome P450 pathway, Claritin can be safety coadministered with other drugs dependent on the P450 pathway. The Claritin approved product labeling does not include any warning or precaution concerning drug interactions resulting in cardiac risks. In fact, to the contrary, the PRECAUTIONS/Drug Interactions Section states that "although increased plasma concentrations...of loratadine...were observed..., there were no clinically relevant changes in the safety profile of loratadine, as assessed by electrocardiographic parameters, clinical laboratory tests, vital signs, and adverse events. There were no significant effects on QTc intervals, and no reports of sedation or syncope."

Pfizer should immediately cease its dissemination and use of all promotional materials for Zyrtec that contain these or similar violations. Pfizer's written response should be received by DDMAC no later than January 6, 1999, and should list all similarly violative materials and a description of its method for discontinuation.

Pfizer's response should be directed to the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17-B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds Pfizer that only written communications are considered official.

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Pfizer Inc.
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In all future correspondence regarding this particular matter, please refer to MACMIS ID# 7035 in addition to the NDA number.

Sincerely,

Joan Hankin, JD
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications